Influenza: epidemiology and hospital management

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Abstract

Influenza is a cause of significant morbidity, mortality, economic and social disruption. Annual seasonal influenza epidemics result in 290,000–650,000 deaths worldwide, while influenza pandemics have resulted in many more – the A(H1N1) pandemic of 1918–1919 caused 20–50 million deaths. Healthcare systems struggle to effectively manage the constant threat because of the evolving nature of the virus. Since the start of 2021, there have been four events of concern related to influenza reported by the World Health Organization. To reduce the burden of disease and protect our global health security, it is essential that clinicians effectively identify and manage cases of influenza, as well as understand and collaborate with the wider public and global health systems. In particular, the rapid identification and management of novel influenza strains of concern is critical. The COVID-19 pandemic has instigated improvements in influenza preparedness guidelines and management protocols. It has accelerated healthcare innovation, with novel tools to manage respiratory disease more effectively. Innovative technologies, new pharmaceuticals and improved global surveillance are changing the way healthcare systems respond to influenza and other diseases to ensure global health resilience and effective management of future outbreaks.

Keywords Disease outbreaks; global health; influenza; pandemics; public health; respiratory tract diseases; respiratory tract infection; vaccines; viruses

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Key points

- Undertake appropriate risk assessment, know the key symptoms and signs for influenza viruses of concern and their specific management, and uphold basic hygiene principles and use of personal protective equipment
- Know how to contact public health professionals (in the UK this is the proper officer at the local council or local health protection team) and inform them of notifiable diseases; if a novel influenza strain is suspected, discuss this with the duty microbiologist/virologist at the nearest specialized laboratory (in England, this is the Public Health England (PHE) Public Health Laboratory)
- Keep up to date with the latest emerging influenza viruses and seasonal strains in your area (e.g. World Health Organization Disease Outbreak News online, PHE website announcement page, ProMED-mail website, HealthMap website)

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has highlighted the importance of effectively managing respiratory disease of pandemic potential. Influenza viruses not only cause high levels of morbidity and mortality seasonally each year, but also present a significant global health security threat. It is critical to understand the pathogenesis and epidemiology of influenza, and to recognize, investigate and manage patients appropriately. At a time when innovation in healthcare is booming, with novel therapeutics and software-based tools to manage respiratory disease, it is important to keep up to date with the latest developments and provide the best possible care to patients. Optimal use of innovative technologies, new pharmaceuticals and improved global surveillance will ensure global health resilience and effective management of future outbreaks.

Pathogenesis and pathophysiology

There are three types of influenza virus that infect humans –A, B and C. Type A viruses are divided into subtypes depending on the type of viral surface glycoprotein –haemagglutinin (H protein) or neuraminidase (N protein). Type B fall into two distinct genetic lineages, Yamagata and Victoria, based on differences in the haemagglutinin glycoproteins. Type A can infect a variety of animals as well as humans; its natural reservoir is aquatic birds. Type B circulates only in humans, and type C can infect humans and pigs, although infections are typically mild.

Influenza evades the immune system by changing its antigenic properties. In *antigenic drift*, small genetic changes occur over time as the virus replicates. The changes are usually so small that the virus's antigenic properties remain the same and the immune system can recognize the pathogen (known as cross-protection). If these small changes accumulate, a virus with different antigens is produced to which the host has no immunity. The population is therefore able to catch flu more than once, and a new flu vaccine is produced each year according to the most prevalent evolving viruses.

In *antigenic shift*, a major genetic change occurs resulting in new H or N proteins. Pandemics are often caused by recombinant viruses that derive some of their genetic material from a non-human influenza virus (e.g. an avian influenza virus) and some from a human influenza virus (known as reassortment). This mixing can occur when a host such as a pig is infected by the two viruses. The H and/or N proteins are derived from the non-human virus and are antigenically different from those the population has immunity to. With a susceptible population, a pandemic can occur. Type A viruses undergo both antigenic drift and antigenic shift, whereas type B viruses change by antigenic drift.

Transmitted by aerosols from an infected individual or from fomites contaminated with respiratory secretions, the influenza virus replicates predominantly in the respiratory epithelial lining of the respiratory tract. Lung inflammation occurs secondary to direct viral infection of the respiratory epithelium and the inflammatory cascade generated by the host immune system.

Epidemiology

Seasonal influenza

Seasonal influenza is a common cause of respiratory infection during the winter months in Northern and Southern Hemispheres, and can occur all year round in tropical and subtropical areas. The disease is frequently mild but can be severe and is a significant cause of mortality in vulnerable individuals, including young children, pregnant women and elderly or immunocompromised individuals.

Annual seasonal influenza epidemics result in around 290,000−650,000 deaths worldwide and infect up to 20% of the population, depending on circulating viral strains.[1] They have a substantial economic impact through reduced workforce productivity and increase pressure on healthcare services.

At the time of writing, there are reduced levels of influenza globally compared with previous years, probably secondary to the non-pharmacological interventions (social distancing, hand hygiene) implemented to reduce severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission. During the first half of March 2021, World Health Organization (WHO) laboratories found 375 positive influenza specimens among 291,427 specimens from 85 countries − 35.2% type A and 64.8% type B.[1] Of the type A viruses, 6.1% were influenza A(H1N1)pdm09 and 93.9% were influenza A(H3N2). All the type B viruses were the B/Victoria lineage.

Influenza pandemics and outbreaks

To date, the only influenza pandemic in the 21st century occurred between 2009 and 2010, caused by the A(H1N1)pdm09 virus and commonly known as swine flu. First identified in Mexico, it was called swine flu because its genetic make-up was derived from a quadruple reassortment involving genes from pigs, birds and humans.[1−3] It mostly caused mild infection because of a level of immunity in the older population so younger persons were disproportionately affected. More than 214 countries were affected, with 284,000 deaths,[3] of which 18,449 were laboratory confirmed.[1] After increasing immunity in the population, the A(H1N1)pdm09 strain is now circulating as one of the seasonal flu viruses and is incorporated into the 2021−2022 Northern Hemisphere recommended vaccine.

During the 20th century, three pandemics occurred − ‘Hong Kong flu’ (A(H3N2)) causing 1−4 million deaths in 1968, ‘Asian flu’ (A(H2N2)), causing a similar number of deaths between 1957 and 1958, and the more severe ‘Spanish flu’ (A(H1N1)), causing 20−50 million deaths in 1918−1919.[1]

Between 2010 and 2020, several cases of human infection from avian influenza strains have been reported, including H5N6, H7N7, H7N3, H7N9, H9N2 and H10N8 strains. H7N9 has been occurring most years since 2013 in humans in China. Since the start of 2021, there have been four events of concern related to influenza reported by the WHO: a case of influenza A(H1N2) variant virus in Brazil with possible links to pig farms; a case of influenza A(H3N2) variant virus in the USA with a link to pig farms; China reported the first case of human infection with avian influenza A(H10N3) virus globally; and India reported a fatal case of influenza A(H5N1) with an unknown source of infection.[1]

Prevention

The WHO convenes consultations in February and September to recommend which strains to include in the vaccines for the Northern and Southern Hemispheres that are developed each year. Influenza types A and B are generally used in the vaccines. Type C strains cause such mild illnesses that they are not included.

For the 2021−2022 Northern Hemisphere influenza season, the following strains have been recommended: two type A strains (A(H1N1)pdm09 and A(H3N2)) and two type B strains (B/Victoria lineage, B/Yamagata lineage). These can be delivered as a quadrivalent vaccine (all four strains) or trivalent vaccine (both type A strains and the B/Victoria lineage).

The vaccines will be available from the autumn to everyone in the UK and are free for front-line health and social care workers, carers, pregnant women, children aged 2−11 years, adults aged 50 and older, those with a long-term health condition and members of a household shielding from COVID-19.[2] The WHO recommends annual vaccination for all high-risk groups and those living and caring for them. Priority should be given to health workers and older adults, followed by pregnant women, children aged 6 months to 5 years, and individuals with chronic health conditions.[1] Vaccination against influenza will be important in 2021−22 as the lack of circulation of influenza during 2020−21 will likely result in a reduced influenza global immunity.

The vaccines should be avoided if a patient has had a serious allergic reaction to the influenza vaccine in the past. As some vaccines are made using eggs, low-egg or egg-free vaccines are available for patients with egg allergies.

Multiple influenza vaccine types are licensed in the UK − inactivated, live attenuated nasal spray, and recombinant. Inactivated vaccines administered via injection are available for adults and children <2 years old. In addition, live attenuated vaccines administered by nasal spray are available for children aged >2 years. In the US, the nasal spray influenza vaccine is approved for people aged between 2 and 49 years old who are healthy and non-pregnant (more information and a list of contraindications can be found here https://www.cdc.gov/flu/prevent/nasalspray.htm). Live attenuated vaccines should not be given to pregnant women and severely immunosuppressed patients.[1,2]

In the UK, children aged between 2 and 17 years old are administered the live attenuated vaccine in the form of a nasal spray. Those aged between 2 and 9 years who have not previously received an influenza vaccine and are in a clinical risk group, should be offered a second dose four weeks later. If the live attenuated vaccine is contraindicated, a quadrivalent inactivated vaccine should be offered. Children aged 6 months to 2 years old who are in a clinical risk group, should be given the quadrivalent inactivated vaccine in the form of an injection, with those who have not received the vaccine previously, receiving a second dose four weeks later.[1,2]

Clinical assessment

This should follow the standard respiratory work-up. Table 1 highlights key symptoms, signs, investigations and management for seasonal influenza, as well as for other influenza viruses, which, while uncommon, are important to detect and manage appropriately. It is important to note that immunocompromised individuals can have atypical presentations.

Seasonal influenza commonly presents with fever, cough (usually dry and can last several weeks) and nasal congestion. Young children can also present with vomiting or diarrhoea.[3] Although most symptoms last for 3−7 days, fatigue and a persistent cough can last 2 or more weeks.[3] Illnesses range from mild to severe and can cause death. Those at risk of severe disease or complications include pregnant women, children <5 years old, elderly individuals and those who have chronic medical conditions or are immunocompromised.[1] Fever is not always present, particularly in elderly people.

Complications of influenza infection include secondary bacterial infection, pneumonia, bronchiolitis, croup, myocarditis, myositis, rhabdomyolysis, encephalopathy, encephalitis, renal failure, respiratory failure, acute respiratory distress syndrome and septic shock.[3]

If uncommon influenza strains are considered, key aspects of the history include the following.

Recent contact with infected persons − spread is generally by close person-to-person contact from respiratory aerosols. Viruses can travel >1 metre to deposit on mucous membranes of the mouth, nose and eyes.[1] Touching an infected surface and then touching these mucous membranes is a common route of transmission. Walking past a person or briefly sitting opposite someone is not considered close contact. Two or more cases within, for example, 2 weeks with an epidemiological link should be thoroughly investigated, especially if they involve healthcare workers or patients in the same ward. Documenting these contacts is important.

Other types of contact − contact within 1 metre of live or dead domestic fowl, wild birds, bird markets, or bird droppings in avian flu, should be noted.[2] Similarly, note contact with pigs in swine flu and consider contact with other animals, exposure in health-care settings and laboratory transmission.

Recent travel − in the 14 days preceding symptom onset, has the patient travelled to any countries with a current or past outbreak? The virus could still be circulating in the human or animal population from past outbreaks.

Onset of symptoms − document symptoms and their onset, including history of fever, cough and shortness of breath. Ask about conjunctivitis that characterises some avian strains.

Table 2 outlines the case definition for possible cases of avian influenza associated with severe human disease, including H7N9, H9N2, H5N1 and H5N6 − one clinical and one exposure criteria must be met.

Illnesses presenting with influenza-like symptoms and which form part of a differential diagnosis include:

- **SARS-CoV-2** − predominantly fever, persistent cough, shortness of breath, anosmia, ageusia.
- **rhinovirus** — predominantly nasal symptoms and less commonly fever, fatigue and myalgia.
- **respiratory syncytial virus** — upper and lower respiratory symptoms; it is a common cause of lower respiratory tract infections in children <1 year old and elderly or immunocompromised individuals.
- **parainfluenza viruses** — mild upper respiratory tract infection, but severe lower respiratory tract infection in immunocompromised patients; a common cause of acute lower respiratory tract infections in young children.
- **adenovirus** - pharyngitis, coryza, fever, malaise, otitis, conjunctivitis, pneumonia, gastrointestinal and nervous system involvement.
- **streptococcal pharyngitis/*Streptococcus pyogenes*** — acute sore throat, with the absence of cough, sneezing and nasal congestion.
- **bacterial meningitis syndromes** — similar symptoms including fever, headache and myalgia. Additional features of meningitis include vomiting, neck stiffness, photophobia, seizures, confusion, purpuric rash and, in children, bulging fontanelles, a blank expression, high-pitched screaming, whimpering and hypotonia.
- **bacterial pneumonia/bronchitis syndromes** — differential or co-infection. Those at increased risk of pneumonia or co-infection include individuals who are elderly, immunocompromised, asthmatic or smokers or have chronic obstructive pulmonary disease.
- **Epstein−Barr virus** — prolonged fever, severe sore throat, fatigue and swollen lymph nodes, seen particularly in young adults.
- ***Bordetella pertussis*** — similar symptoms to influenza but with the characteristic cough.

Investigations

If influenza is circulating in the community and there are no features of complications, diagnosis is generally made on clinical features. To determine community circulation in the UK, weekly reports of influenza, flu-like illness, and respiratory disease, including COVID-19, are published online.[4] In a hospital setting, laboratory diagnosis is important to appropriately isolate cases and prevent spread of infection. Table 1 highlights

Influenza viruses — key symptoms, signs, investigations and management[1–5]

Virus	Symptoms	Signs	Investigations	Management
Seasonal influenza	• Incubation period 1–4 days • Increased suspicion during winter season, if current outbreak and in unvaccinated individuals • Myalgia, arthralgia, lethargy, headache, malaise • Dry cough that can last for 2 or more weeks • Sore throat, nasal congestion, rhinorrhoea • Diarrhoea, abdominal pain, nausea, vomiting more common in children	• Fever >38°C • Mild cervical lymphadenopathy, more common in children • In children: tachypnoea, conjunctival erythema, nasal oedema, hyperaemia of oropharynx	• Diagnosis based on signs and symptoms • Nasopharyngeal swab, particularly if high risk of complications, in high-risk groups and hospitalized patients • Rapid diagnostic test can be appropriate — around 70% sensitive and 90% specific • Chest X-ray usually normal, infiltrates suggest pneumonia	• Seasonal influenza vaccination, especially for high-risk groups • Most recover without needing medical attention within 1 week • Antipyretics/analgesics, encourage fluids • For hospitalized patients or individuals at risk of complications or in an at-risk group, if influenza is circulating in the community, and treatment can be started within 48 hours of symptom onset (36 hours for zanamivir in children), give neuraminidase inhibitors,[a] and follow guidance[d,e] • Resistance to adamantanes • Post-exposure prophylaxis with neuraminidase inhibitors;[a] if influenza is circulating, and close contact with case, and in at-risk group and not immunized and follow guidance[e,f]
A(H5N1)	• Incubation period 2–5 days, ranging to 17 • Can present with mild to severe symptoms • Contact history with birds or close contact with a case • History of travel[b] • Dry or productive cough • Dyspnoea • Malaise and myalgia • Progress to severe lower respiratory tract disease during days 3–6 in many • Abdominal pain, diarrhoea and vomiting associated with HPAI H5N1 • Can progress quickly to ARDS, multiorgan failure • Reported complications: encephalitis, altered mental state, seizures, spontaneous abortion • Sore throat and coryza less common	• Fever >38°C • Hypoxaemia • Tachypnoea • Rales, wheezing, and focal decreased breath sounds on auscultation • Multiple organ dysfunction • Secondary bacterial and fungal infection • 53% case fatality rate	• Nasopharyngeal and throat swab or endotracheal aspirate if intubated (rapid diagnostic tests are inappropriate) • Chest X-ray can be normal or show pneumonia-like infiltrates • Blood tests: severe cases can show leukopenia, lymphopenia and mild to moderate thrombocytopenia, elevated AST/ALT	• Isolate the patient and use PPE • If meets case definition for avian influenza, start oseltamivir immediately (before a laboratory diagnosis). Dosages for the treatment of seasonal influenza are appropriate for initiating treatment; follow guidance[d,e,g] • Post-exposure prophylaxis with neuraminidase inhibitors;[a] follow guidance[g] • Corticosteroids not recommended unless adrenal insufficiency or refractory septic shock • A(H5N1) vaccines been developed and licensed around the world, including Europe and the USA, for use in pandemic situations

A(H7N9)	• Incubation period 1–10 days, average 5 • Can present with mild to severe symptoms • Contact history with birds/poultry or close contact with a case • History of travel[c] • Dry or productive cough • Dyspnoea • Some have headache, myalgia, fatigue, diarrhoea or vomiting; sore throat less likely • Progress to severe lower respiratory tract disease during days 3–6 in many, multiorgan dysfunction/failure, ARDS • Reported complications: haemophagocytosis, shock, DIC • Atypical presentations: mental status, seizures and febrile diarrhoeal illness progressing to pneumonia	• Fever >38°C • Hypoxaemia • Tachypnoea • Rales, wheezing, and focal decreased breath sounds on auscultation • Multiple organ dysfunction • Secondary bacterial and fungal infection • Clinical findings similar to community-acquired pneumonia • 39% case fatality rate	• Nasal, nasopharyngeal or oropharyngeal swab or endotracheal aspirate if intubated (rapid diagnostic tests are inappropriate) • Chest X-ray can be normal or show pneumonia-like infiltrates • Blood tests: can have normal white cell count or mild leukopenia, lymphopenia and mild to moderate thrombocytopenia; elevated AST/ALT	• Isolate the patient and use PPE • If meets the case definition for avian influenza, start oseltamivir immediately (before a laboratory diagnosis). Dosages for the treatment of seasonal influenza are appropriate for initiating treatment, follow guidance[d,e,g] • Post-exposure prophylaxis with neuraminidase inhibitors.[a] Because of oseltamivir resistance seen in H7N9, use a treatment dose, follow guidance[g] • Resistance shown to adamantanes • Corticosteroids not recommended unless adrenal insufficiency or refractory septic shock • Vaccines are being developed; none are licensed

ALT/AST, alanine/aspartate transaminase; ARDS, acute respiratory distress syndrome; DIC, disseminated intravascular coagulation; HPAI, highly pathogenic avian influenza; LDH, lactate dehydrogenase.

[a] Oseltamivir (Tamiflu) and zanamivir (Relenza) in the UK. In certain countries, other neuraminidase inhibitors are licensed. Oseltamivir is on the WHO List of Essential Medicines. Because of high resistance to adamantane antiviral drugs (e.g. amantadine, rimantadine), the WHO does not recommend their use for monotherapy.

[b] Countries with a known occurrence of 'high consequence infectious disease' (updated 21 March 2020) include Bangladesh, Cambodia, China, Egypt, Indonesia, Nepal and Vietnam (UK government; https://www.gov.uk/guidance/high-consequence-infectious-disease-country-specific-risk#history).

[c] Countries with a known occurrence of 'high consequence infectious disease' (updated 21 March 2020) include China (https://www.gov.uk/guidance/high-consequence-infectious-disease-country-specific-risk#history).

[d] Treatment of influenza NICE guidance: https://cks.nice.org.uk/topics/influenza-seasonal/management/treating-influenza/

[e] Treatment of influenza PHE guidance: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/833572/PHE_guidance_antivirals_influenza_201920.pdf.

[f] Post exposure prophylaxis NICE guidance: https://cks.nice.org.uk/topics/influenza-seasonal/management/post-exposure-prophylaxis/

[g] Treatment of possible human cases of avian influenza viruses PHE guidance: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/857436/Avian_flu_human_cases_guidance_Jan2020.pdf

Table 1

Case definition for possible cases of avian influenza associated with severe human disease

Clinical criteria

a) Fever ≥38°C *and* lower respiratory tract symptoms (cough or shortness of breath) or chest radiograph findings of consolidation or acute respiratory distress syndrome

or

b) Other severe/life-threatening illness suggestive of an infectious process

Exposure criteria

(1) Close contact (within 1 metre) with live, dying or dead domestic poultry or wild birds, including live bird markets, in an area of the world affected by avian influenza or with any confirmed infected animal, in the 10 days before the onset of symptoms

or

(2) In the 10 days before the onset of symptoms, close contact with:

- a confirmed human case of avian influenza or
- human case(s) of unexplained illness resulting in death from affected areas or
- human case(s) of severe unexplained respiratory illness from affected areas

Source: From Public Health England guidance (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/857436/Avian_flu_human_cases_guidance_Jan2020.pdf) on 'Investigation and initial clinical management of possible human cases of avian influenza viruses that have been associated with severe human disease, v2, 2020'.

Table 2

the investigations that are most useful for specific influenza infections.

Investigations specific to influenza include:

- nasopharyngeal swab, nasal wash, bronchial wash, nasal aspirate or sputum sample tested for presence of influenza A and B viruses using direct immunofluorescent antibody staining, reverse-transcriptase polymerase chain reaction, enzyme immunoassay or viral culture (often used for screening).
- serology and rapid diagnostic tests.
- chest radiograph, which appears normal in uncomplicated cases; it is important to perform this to exclude complications such as pneumonia.
- serial samples of blood or bodily fluids, which can help demonstrate viral shedding patterns or treatment effect.
- follow local microbiological or public health guidance, consider investigations to identify complications and support differential diagnoses, for example blood cultures, sputum Gram staining and *Legionella* and *Streptococcus pneumoniae* urinary antigen testing.

If a novel influenza strain is suspected (i.e. avian or swine influenza), the case must be discussed with the duty microbiologist/virologist at the nearest specialized laboratory (in England, this is the Public Health England (PHE) Public Health Laboratory). If testing is indicated, the treating clinician must then also notify local public health professionals (in the UK this is the proper officer at the local council or local health protection team). In the UK, the public health laboratory will specify which samples should be taken and orchestrate the sample transportation to the assigned specialized testing laboratory.

Management

Patients should wear a face mask or cough and sneeze into a tissue, throw it into a non-touch bin and maintain strict hand hygiene. Individuals coughing in waiting areas can be given a mask and invited to sit more than a metre away from others. Patients suspected of having a severe respiratory virus infection (e.g. avian influenza) should be placed in isolation, ideally under negative pressure. Contacts should be immediately identified, monitored (particularly for fever) and evaluated. Healthcare professionals should uphold infection control practices, including strict hand hygiene, thorough cleaning of surfaces and wearing personal protective equipment (PPE) — a gown, gloves and face mask (fitted FFP3 respirator) with eye protection.

Treatment of influenza cases should include standard respiratory management, including correcting hypoxia, encouraging oral intake and giving pain relief. Table 1 summarizes management for the most common influenza strains.

For seasonal influenza, antivirals are not usually recommended for otherwise healthy individuals. If influenza is circulating in the community and treatment can be started within 48 hours of symptom onset (36 hours for zanamivir in children), individuals at risk of complications or in an at-risk group should be prescribed oral oseltamivir (inhaled zanamivir if there is a risk of oseltamivir resistance, e.g. A(H1N1), or as second-line treatment).[4,5]

Groups considered at-risk for seasonal influenza are:

- individuals with chronic respiratory, heart, kidney, liver or neurological disease, or diabetes mellitus and those who are obese or immunosuppressed.
- adults aged >65 years.
- children <6 months old.
- women who are pregnant or up to 2 weeks post-partum.

Antivirals can be given as post-exposure prophylaxis if an individual has been in close contact with someone with influenza-like symptoms while influenza is circulating in the community, and the individual is in an at-risk group and has not been effectively immunized. Treatment should be started within 48 or 36 hours of this contact for oseltamivir and zanamivir, respectively.[4,5]

Consider hospital admission if an individual presents with complications (e.g. pneumonia) or has an illness that could be affected by influenza (e.g. type 1 diabetes), or a serious influenza strain or serious differential is being considered.

If an individual meets the case definition for avian influenza outlined in Table 2, start oseltamivir immediately before being given a laboratory diagnosis. Dosages for the treatment of seasonal influenza are appropriate for initiating treatment of avian influenza cases.[4] In England, a PHE-led incident management team will guide the management of contacts of presumptive positive/confirmed cases of avian influenza. Because of the oseltamivir resistance seen in H7N9, a treatment dose instead of a post-exposure prophylactic dose is recommended for contacts.[4]

In the UK, influenza is a notifiable disease, and it is a statutory duty to report suspected disease to the proper officer at the local council or local health protection team (officers are listed at www.gov.uk/health-protection-team). A notification form (www.gov.uk/government/publications/notifiable-diseases-form-for-registered-medical-practitioners) should be sent to the proper officer within 3 days, or they should be phoned within 24 hours if the case is urgent. Clinical suspicion is sufficient and a laboratory diagnosis not required.[4] Under the International Health Regulations (2005), cases of avian influenza A viruses should be reported to the WHO.

Research and innovation

The COVID-19 pandemic has accelerated innovation in the fields of public health and virology. Specifically, the digital delivery of healthcare is growing and becoming part of the future of care. Global data-sharing and improved surveillance are the cornerstones of managing an outbreak.

For improved disease surveillance, it is necessary to have secure data sharing platforms with incentives for researchers, laboratories, and surveillance centres to share data. The WHO Pandemic Influenza Preparedness (PIP) Framework brings together key stakeholders in a global approach to pandemic influenza preparedness and response. Under this framework, the Global Influenza Surveillance and Response System (GISRS) forms an international network of laboratories that undertake surveillance and sharing of influenza strains. In addition, the Nagoya Protocol promotes the fair and equitable sharing of benefits arising from the use of genetic resources. The COVID-19 pandemic highlighted some of the challenges in data sharing and prompted the establishment of the WHO BioHub System. The System enables WHO Member States to safely, transparently, and voluntarily share novel biological materials. Materials with epidemic or pandemic potential will be shared using BioHub designated laboratories. This new system is being piloted during 2021 with COVID-19 as a test case.

Wearable sensors such as Fitbits®, monitoring resting heart rate and sleep measurements, have improved influenza-like illness predictions and could be used for timely outbreak response. Machine learning has been used to provide real-time and forecasted estimates of influenza activity using information from Google searches, Twitter microblogs, hospital visit records and data from other surveillance systems. This methodology has been shown to outperform standard prediction models and forecast 3 weeks in advance with good accuracy.

Increased use of telemedicine services and contact-tracing applications are changing the management of respiratory infections. Online consultations have become commonplace secondary to the necessity imposed by the COVID-19 pandemic. The demand for telemedicine is anticipated to continue beyond the pandemic, driven by patient and clinician demand. In private healthcare systems, many insurance companies appreciate the financial incentive of the digital first approach and there has been a significant increase in investment funding of emerging telemedicine companies around the world.

The technology applied to COVID-19 detection, therapeutics and vaccines is now being tested on influenza. mRNA vaccines against various influenza strains are being tested in early clinical trials, and an increasing number of pharmaceutical companies are registering clinical trials.

This new wave of technological growth also highlights the challenges of data ownership and data protection for patients. The COVID-19 pandemic demonstrated the importance of trust between communities and governments with regards to the handling of personal data. Overcoming fragmented databases, inaccurate data, and data interoperability will be critical for harnessing the potential of digitalisation.

The management of influenza is likely to change rapidly over the next few years as the adoption of technology necessitated by the COVID-19 pandemic begins to find new applications and healthcare systems adapt to become more efficient and better at protecting our global health security. ◆

KEY REFERENCES

1 World Health Organization. Available from: http://www.who.int [Accessed 31 August 2021].

2 National Health Service Choices. Available from: http://www.nhs.uk [Accessed 31 August 2021].

3 Centers for Disease Control. Available from: http://www.cdc.gov [Accessed 31 August 2021].

4 Public Health England. Available from: http://www.gov.uk/government/organisations/public-health-england [Accessed 31 August 2021].

5 Clinical Knowledge Summaries National Institute for Health and Care Excellence. Available from: http://cks.nice.org.uk/topics/influenza-seasonal/ [Accessed 31 August 2021].

TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A 35-year-old woman presented with a fever and dry cough. Her symptoms had started 3 days after returning from a business trip to Beijing, China. In this scenario, A(H3N2) is currently circulating as seasonal influenza in 60% of cases and A(H1N1) in 40% of cases.

On clinical examination, her temperature was 38.5°C, heart rate 110 beats/minute, blood pressure 135/85 mmHg, respiratory rate

20 breaths/minute, and oxygen saturations 95% on air. Chest auscultation was clear, and the abdomen was soft and non-tender.

What is the most likely influenza strain responsible for her symptoms?

A. A(H1N1)
B. A(H5N1)
C. A(H10N3)
D. A(H3N2)
E. A(H7N9)

Question 2

A 50-year-old male ornithologist presented with a fever, malaise, lethargy and a persistent non-productive cough. A week previously, he had returned from a nine-month backpacking holiday, during which he visited Australia, Brunei, Cambodia, China, Japan, Laos, Malaysia, Mongolia, New Zealand, and Papua New Guinea.

On clinical examination, his temperature was 39.0°C, heart rate 120 beats/minute, blood pressure 110/79 mmHg, respiratory rate 18 breaths/minute, and oxygen saturations 90% on air. He had widespread crackles and wheezing on auscultation of his chest. A SARS-CoV-2 PCR was negative.

After isolation and standard management for respiratory presentations, what is the next most important action?

A. Give oseltamivir
B. Discuss with the duty microbiologist/virologist at the nearest specialized laboratory e.g. the Public Health England Public Health Laboratory
C. Notify the local public health professionals, e.g. the proper officer at the local council or local health protection team
D. Initiate contact tracing
E. Take nasopharyngeal and throat swabs

Question 3

A 66-year-old man presented as an emergency with a 1-day history of dry cough, sore throat and a fever. Seasonal influenza is circulating in the community.

What prescribing decision should be taken?

A. Do not administer any antivirals
B. Give oral oseltamivir
C. Give inhaled zanamivir
D. Give inhaled oseltamivir
E. Give oral zanamivir

